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Letters to the Editor

BREAST CANCER, CIGARETTE SMOKING, AND PASSIVE SMOKING

In recent papers on cigarette smoking and breast cancer (1–6), as in all earlier such papers, the reference category was women who had never smoked. Yet there is evidence, some published, some unpublished, that passive smoking among never smokers could increase breast cancer risk. Thus, a better reference category for these studies may be women who never smoked and who have no reported exposure to environmental tobacco smoke.

Hirayama (7) has mentioned breast cancer as possibly associated with passive smoking. For this communication, Dr. Hirayama (personal communication, 1988) has provided detailed mortality data (table 1) for never smoking women according to husband's smoking habit. The data show an elevated risk of breast cancer in never smokers whose husbands smoked. Sandler et al. (8–10) report an association between passive smoking and breast cancer. Data provided by Dr. Sandler (personal communication, 1986) also show an increased risk of breast cancer in never smoking women whose husbands smoked (table 2). Miller (11) also reported an association of passive smoking with breast cancer. Horton (12) correlated male lung cancer incidence with female breast cancer incidence in various countries and various parts of the United States, also suggesting that ambient tobacco smoke may be related to breast cancer.

A reasonable estimate for the relative risk of passive smoking breast cancer based on both the Hirayama and Sandler data sets would be about 1.4 for all ages combined. For women under 50 years of age, considering the known lag time between incidence and death, the best estimate for relative risk is about two. The fraction of never smoking women exposed passively to smoke can be estimated as follows. The fraction of controls living with smokers in all 14 US passive smoking studies through 1987 (13) is 60 percent. Friedman et al. (14) indicate that, additionally, 40 percent of nonsmoking women married to nonsmoking husbands are exposed to ambient tobacco smoke. Thus the total percent exposed would be 60% + 0.40 × 40% = 76%. The estimated relative risk of breast cancer for all never smokers compared with nonexposed never smokers would then be 1.3 (1.4 × 0.76 + 1.0 × 0.24), and the incidence risk for those under age 50 would be about 1.8 (2 × 0.76 + 1.0 × 0.24).

If we consider as an example the study by Rohan and Baron (1) of breast cancer and active smoking, we can show the effect of a passive smoking adjustment on their data for current smokers (all ages) (table 3). The odds ratio for breast cancer in active smokers is raised from a nonsignificant 1.3 to a statistically significant 1.7. The premenopausal odds ratio for breast cancer for currently smoking women in Rohan and Baron's table 3 would likewise be adjusted upward from 1.32 to 2.4 (1.32 × 1.8).

The results in the various papers on active smoking and breast cancer are at best confusing. However, adjusting for a presumed association of passive smoking with breast cancer would elevate probably all of the smoking relative risks to a level greater than unity. Averaging the rather scattered results for the six studies cited (1–6) yields excess risks for current smokers that are about twice those for passive smokers and ex-smokers. Such a result is consistent with one of the explanations proposed by Rohan and Baron, namely that the results reflect an unstable balance between direct (carcinogenic) and indirect (hormonal) effects, but with the added thought that the protective hormonal effects are greater at the higher levels of exposure. An additional possibility is that most of the breast carcinogenic damage may be coming from vapor phase constituents in the cigarette smoke. Recent evidence (15) indicates that 70 percent of the tar in environmental tobacco smoke is in the vapor phase, whereas all of the tar in direct smoking is in the particulate phase. Particulate phase smoke tends to be cleared into the mouth and swallowed, while vapor phase constituents absorb into the blood and lymph systems. This may mean that, unlike lung cancer, breast cancer effects from direct smoking may be coming primarily from the va-

TABLE 1. Relative r
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Husband's age at enrollment (years)	
40–49	
Cases	
Population	
50–59	
Cases	
Population	
60–69	
Cases	
Population	
70–79	
Cases	
Population	
Total, all ages	
Cases	
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* Case and populati

TABLE 2. Relative ris
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Source: https://www.industrydocuments.ucsf.edu/docs/yxyx0000

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SMOKING

+ 0.40 × 40% = 76%.
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TABLE 1. Relative risk of mortality for breast cancer in never smoking women, by age group and smoking habit of the husband, in a prospective study in Japan, 1966–1981*

Husband's age at enrollment (years)	Husband's smoking habit (no. of cigarettes per day)						Relative risk, husband an ever smoker	95% confidence interval
	Ex-smoker	1–14	15–19	20+	Ever smoker	Never smoker		
40–49								
Cases	1	12	4	7	24	4	1.5	0.5–4.2
Population	1,255	8,621	5,158	10,764	25,798	6,229		
50–59								
Cases	5	15	3	20	43	8	1.6	0.8–3.5
Population	1,922	9,668	4,052	9,820	25,462	7,791		
60–69								
Cases	2	8	2	10	22	9	1.0	0.5–2.1
Population	2,687	7,243	2,513	4,651	17,094	7,120		
70–79								
Cases	1	0	0	2	3	2	0.9	0.2–5.2
Population	348	612	105	226	1,291	755	—	—
Total, all ages								
Cases	9	35	9	39	92	23	1.26	0.8–2.0
Population	6,212	26,144	11,828	25,461	69,645	21,895		

* Case and population data are from a personal communication from Dr. Hirayama.

TABLE 2. Relative risk of breast cancer in never smoking women, by age and menopausal status and by smoking habit of husband, in a case-control study in North Carolina, 1979–1981*

Wife's age at interview (years)	Husband's smoking habit		Odds ratio	95% confidence interval
	Ever	Never		
<40				
Cases	4	2	4.4	0.9–23.1
Controls	24	53		
40–49				
Cases	9	4	2.9	0.7–11.0
Controls	15	19		
50–59				
Cases	6	4	1.1	0.3–4.5
Controls	27	20		
60+				
Cases	0	3	0.0	
Controls	10	9	—	—
Totals, all ages				
Cases	19	13	1.94	0.9–4.2
Controls	76	101		
Premenopausal				
Cases	6	2	7.1	1.6–31.3
Controls	27	64		
Postmenopausal				
Cases	13	11	0.9	0.4–2.2
Controls	49	37		

* Case and control data from a personal communication from Dr. Sandler.

TABLE 3. The effect of adjustment for passive smoking on current smoking risk for breast cancer in table 2 of Rohan and Baron (1)

	Smoking status		Never smoked, based on 76% passively exposed	
	Current smoker	Never smoked	Exposed	Not exposed
Cases	108	254	201	53
Controls	88	273	199	74
Total	196	527	400	127
Crude odds ratio vs. never smoked	1.32	1.00	1.09	0.77
95% confidence interval	0.95–1.83		0.84–1.41	0.52–1.14
Crude odds ratio vs. nonexposed never smoked	1.71	1.30	1.41	1.00
95% confidence interval	1.09–2.69	0.88–1.92	0.94–2.11	

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por phase smoke, in other words, more from the smoker's passive smoking than from the smoke directly inhaled from the cigarette.

The intent of this letter is not to "prove" an association between breast cancer and passive or direct smoking. Rather, it is to alert researchers in the breast cancer field to consider seriously, as a reference category in future studies, the use of never smokers who have had little or no exposure to environmental tobacco smoke. Considering the long induction periods involved in breast cancer, it will be necessary to trace histories of passive exposure over long periods of time in order to get meaningful data. Only by performing such investigations can we determine the real risk, if any, of breast cancer from various degrees of passive smoking and thus determine the real risk, if any, from direct smoking.

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✓ *COMMENT BY DR. SANDLER*

While many will not be convinced of the biologic plausibility of a breast cancer risk from passive smoking, the example provided by Wells (1) illustrates the potential hazard of dismissing, a priori, the possibility of such an effect. His argument holds for other conditions which may later be found to be smoking-related, and points to the need for identifying truly unexposed comparison groups in epidemiologic studies.

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RE: "WARTIME DETERMINANTS OF ARTERIOGRAPHICALLY CONFIRMED CORONARY ARTERY DISEASE IN BEIRUT"

Sibai et al. (1) have reported associations between exposure to both acute and chronic war events and artiographically confirmed coronary artery disease. They indicate that the significant associations were consistent using both the arteriography series approach of separating cases

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